Natural History of apnea associated with periventricular intraventricular hemorrhage (PIH)

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It has been our observation that the apnea associated with PIH is generally unresponsive to treatment. The purpose of this study was to systematically observe the natural history, response to theophylline treatment, and the outcome of these apneas in relation to the severity of PIH.

Materials and Methods: Infants with a birth weight of less than 1500 gm who had at least three recurrent apneas per day were included in this study. Apnea was defined as a cessation of respiration longer than 20 seconds or if accompanied by a decrease in heart rate under 80 beats per minute with or without cyanosis. All infants under study were evaluated with cardio-respiratory monitor (Hewlett Packard Neonatal Monitor). Trained NICU nursing staff confirmed apneic spells by physical examination. Criteria for theophylline treatment included: 1). no identifiable cause of apnea other than prematurity with or without PIH, 2). at least 3 recurrent episodes of apnea defined as above within a 24 hour period. Theophylline was administered intravenously at a loading dose of 6mg/kg/dose followed by 2mg/kg every 12 hours. Serum theophylline concentration was determined at trough level twice a week. Theophylline treatment was continued until apnea no longer occurred for at least one week. All infants had real time cranial ultrasound studies on admission, daily for 7 days and twice weekly thereafter. Grading of the severity of PIH follows that of Papile.(1).

Results: During a one year period (1981-'82), 22 of 53 outborn VLBW infants were studied. Table I compares two groups of apneic infants, 14 with PIH (PIH group) 8 without PIH (No PIH group). Birthweight, gestational age and serum theophylline levels were similar. Apnea ceased to occur within 48 hours of theophylline treatment in 6 of 8 infants (75%) in No PIH group, while none of the PIH infants responded within the same period of treatment. ($P<0.001$). The mean duration of the refractory period was significantly longer in PIH group compared to No PIH group (26±18 days vs 4.4±7 days, $P<0.002$).

Serial echoencephalographic pictures were reviewed and the date of complete disappearance of echodensity (hemorrhage or blood clot) was determined. Table II shows the grading of IVH, the age of disappearance of echodensity and the age apnea ceased to occur in 8 patients. Recurrent apnea associated with IVH ceased to occur at approximately the time the echodensity disappeared. The time of cessation of apnea was approximately two and a half days prior to the disappearance of the echodensity.

Summary: Apnea associated with PIH is recurrent in nature and does not respond to theophylline treatment. It will likely stop at the time when echodensity disappears from the ventricles of brain substance. This implies that the more extensive the PIH is, the longer the apnea persists.

Table I. EFFECT OF THEOPHYLLINE ON APNEA WITH & WITHOUT PIH

	No	GA(wk)	B.W.(gm)	Theo Level (mg%)	Apnea Stop in 48 hrs	Refractory days
PIH	14	29±2	1064±225	11±3	0(%)	26±18
No PIH	8	29±1	1099±241	10±3	6(75%)	4.4±7
Stud †	P	NS	NS	NS	<0.001*	<0.002

*Fischer Exact Test

Table II. TIMING OF DISAPPEARANCE OF ECHODENSITY & APNEA

Pt.	IVH Grade	Age(days) Echodensity Disappeared	Age(days) Apnea Ceased	Chronological Difference (days)
1	1	13	10	-3
2	1	35	26	-9
3	1	20	26	+6
4	1	23	18	-5
5	11	17	16	-1
6	11	42	41	-1
7	111	55	46	-9
8	IV	23	24	+1
		m=28.5	m=25.9	m=2.6 days

Reference: 1. Papile L, et al: Incidence & evaluation of subependymal and intraventricular hemorrhage: A study of infants with birth weight less than 1500 gm. J. Pediat. 95:529, 1978.

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